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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,510	05/16/2006	John Michael Beals	X-16280	7502

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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
06/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,510	BEALS ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-56* is/are pending in the application.

4a) Of the above claim(s) *42-48,52 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-51 and 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-41 have been canceled and claims 42-56 were added in the amendment filed 09 February 2007. Claims 42-56 are currently pending.

Election/Restrictions

Applicant's election without traverse of Group III in the reply filed on 26 February 2008 is acknowledged.

Claims 42-48, 52 and 56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 26 February 2008. Claims 49-51 and 53-55 are currently under examination in the instant Office action.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

It is noted that this application appears to claim subject matter disclosed in prior Application No. PCT/US04/037200 filed 12 January 2004. A reference to the prior application must be inserted as the first sentence(s) of the specification of this

application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. **If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application**. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless

previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 16 May 2006 is in compliance with the provisions of 37 CFR 1.97 and has been considered by the examiner.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other

information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-51 and 53-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a mutein of human FGF-21 "consisting of human FGF-21 containing 1 or 2 engineered disulfide bonds". However, the recitation of "engineered disulfide bonds" implies much more than what seems to be the intent of the instant specification. The specification appears to be directed to adding additional disulfide bonds by introducing additional cysteine residues at particular amino acid positions in the FGF-21 molecule. At page 10 of the specification, it appears that the purpose of the additional bonds would be to constrain the flexibility of the 118-134 amino acid loop of FGF-21 in order to enhance the physical stability of the prpotein in

the presence of a preservative. But, as the claims are currently drafted, the orientation of the disulfide bonds is not limited to any particular pairing. If the cysteine bonds are "engineered", this could encompass pairing of different cysteines in different orientations, such that one would end up with a variety of FGF-21 molecules with different structural orientations, with various bond lengths. This could result in molecules which are so folded that they no longer have biological activity. Therefore, the claims lack a written description of the subject matter which is being claimed.

Claims 49-51 and 53-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutein of human FGF-21 containing an additional disulfide bond wherein cysteine is substituted for L118 and A134 and wherein these additional cysteine residues form a disulfide bond, does not reasonably provide enablement for "1 or 2 engineered disulfide bonds". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As pointed out above, the recitation of "engineered disulfide bonds" is not limited to introduction of cysteine residues and pairing of the disulfide bonds between particular amino acids. If cysteine residues are introduced at 4 of the recited positions in the claims (i.e. leucine 21, alanine 26, leucine 33 and alanine 134), this would allow for disulfide bond formation between 21 and 26, 33 and 134, 21 and 33, 26 and 134, 21 and 134, and 26 and 33. This will result in disulfide bonds between various cysteines (including possibly bonding with the naturally occurring cysteine molecules in the native

sequence) with very different conformations and different bond lengths. Not all of these proteins would be expected to retain biological activity based on the changes in the conformation of the protein. Furthermore, not all of the molecules that could be formed would be expected to have the increased stability that is the aim of the modification according to the specification. Therefore, the claims are much broader than the enabling disclosure for the reasons given above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 49-51 and 53-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-27 of copending Application No. 11/571,933. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '933 include the

same mutations which are being claimed in the instant application. Therefore, the instant claims would be obvious over the claims of '933 because it would routine to make a mutein with one set of mutations (i.e. the cysteine mutations) without the inclusion of the Leu 153 mutation which is disclosed and claimed in '933.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 49-51 and 53-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-30 and 32-35 of copending Application No. 11/574,332. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '332 include the same mutations which are being claimed in the instant application. Therefore, the instant claims would be obvious over the claims of '332 because it would routine to make a mutein with one set of mutations (i.e. the cysteine mutations) without the inclusion of the Ser 167 mutation which is disclosed and claimed in '332.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 49-51 and 53-55 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-23, 25-27, 29-31 and 33-35 of copending Application No. 11/718,636. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of

'636 include the same mutations which are being claimed in the instant application. Therefore, the instant claims would be obvious over the claims of '636 because it would routine to make a mutein with one set of mutations (i.e. the cysteine mutations) without the inclusion of the Asn 121 and/or Ser 167 mutation which is disclosed and claimed in '636.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on Monday-Friday, 6AM-2PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine J Saoud/
Primary Examiner, Art Unit 1647